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Decreases in antimicrobial use associated with multihospital implementation of electronic antimicrobial stewardship tools

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Preliminary versions of this work were presented at IDWeek 2016 (abstract 963) and IDWeek 2017 (abstract 1633).

Key points: Steward participation in implementation and development of comparative antimicrobial use visualization tools and monthly learning collaboratives were associated with reductions in inpatient total and anti-

pseudomonal antimicrobial use at eight Veterans Affairs (VA) facilities relative to the rest of the VA.

Key words: antimicrobial stewardship, antibiotic utilization, data visualization

Abstract:

Background: Antimicrobial stewards may benefit from comparative data to inform interventions that promote optimal antimicrobial use in the inpatient setting.

Methods: Antimicrobial stewards from eight geographically dispersed Veterans Affairs (VA) inpatient facilities participated in the development of iterative antimicrobial use visualization tools that allowed for comparison to facilities of similar complexity. The visualization tools consisted of an interactive web-based antimicrobial dashboard and, later, a standardized antimicrobial usage report updated at user-selected intervals. Following tool implementation, stewards participated in monthly learning collaboratives. The percent change in average monthly antimicrobial use [all antimicrobial agents, anti-methicillin-resistant *Staphylococcus aureus* agents (anti-MRSA), and anti-pseudomonal agents] was analyzed using a pre-post (1/2014-1/2016 versus 7/2016-1/2018) design with segmented regression and external comparison with uninvolved control facilities ($n=118$).

Results: Intervention sites demonstrated a 2.1% decrease (95% confidence interval (CI) [-5.7%, 1.6%]) in total antimicrobial use pre-post intervention, versus a 2.5% increase (95% CI [0.8%, 4.1%]) in non-intervention sites (absolute difference 4.6%, $P=0.025$). Anti-MRSA antimicrobial use decreased 11.3% (95% CI [-16.0%, -6.3%]) at intervention sites versus a 6.6% decrease (95% CI [-9.1%, -3.9%]) at non-intervention sites (absolute difference 4.7%, $P=0.092$). Anti-pseudomonal antimicrobial use decreased 3.4% (95% CI [-8.2%, 1.7%]) at intervention sites versus a 3.4% increase (95% CI [0.8%, 6.5%]) at non-intervention sites (absolute difference 7.0%, $P=0.018$).

Conclusions: Comparative data visualization tool use by stewards in a pilot implementation project at eight VA facilities was associated with significant reductions in overall antimicrobial and anti-pseudomonal use relative to uninvolved facilities.

Introduction:

Inappropriate antimicrobial prescribing, which accounts for 30-50% of all use, is a major driver of increased antimicrobial resistance, *Clostridioides difficile* infection, and other adverse events and unnecessary health care costs (Fridkin vital signs PMID 24598596; Fleming-Dutra JAMA PMID 27139059). Antimicrobial stewardship programs (ASPs) strive to improve antimicrobial use by encouraging evidence-based decisions regarding choice and duration of therapy [1].

Antimicrobial stewards have long lacked the ability to compare their antibiotic usage to either national norms or to comparable facilities. In this regard, the development of Standardized Antimicrobial Administration Ratios (SAARs) within the Antimicrobial Use (AU) Option of the National Health Safety Network (NHSN) by the Centers for Disease Control (CDC) has been a major advance. These reports provide participating sites with facility-level measures of days of therapy per 1000 patient days present (DOT/1000 DP) and utilize indirect standardization techniques to represent antimicrobial use data as observed to expected ratios based on CDC modeling criteria [2]. However, the NHSN reports do not provide direct information regarding where an institution's antimicrobial use lies in relation to similar facilities and do not demarcate antimicrobial use according to specific diagnoses or across the temporal course of therapy from initiation of empiric therapy through de-escalation and subsequent discharge. Such information as to how (vs. how

much) antibiotics are used can supplement information regarding antibiotic usage patterns.

To address this information gap, we extended previous projects [3,4] that extracted inpatient antimicrobial use data from the VA's Corporate Data Warehouse (CDW) to develop a suite of interactive graphic tools that provide stewards with in-depth facility-level reports of antibiotic use. Antimicrobial use at the dashboard user's (e.g. steward's) facility can be compared to all VA facilities or user-selected facilities of similar complexity levels, and plots of the system-wide variability of antimicrobial use are provided. We pilot tested the usability of these graphic tools and assessed their impact on three important antimicrobial use metrics at eight VA healthcare facilities.

Methods:

Electronic antimicrobial graphic tool development:

Specifying targeted infectious diseases and creating a framework for inpatient antimicrobial time course

We initially constructed the antimicrobial use displays according to two dimensions: disease and time frame within hospitalization. For the disease dimension, we focused on three common infectious conditions: *Pneumonia*, *Urinary tract infection*, and *Skin/soft tissue infection (PUS)*. Diagnoses were determined by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)[5] and cross-mapped ICD-10-CM codes⁷ for each infectious process at hospital admission and discharge, as identified by

a combination of (1) those identified previously in the literature [7], and (2) those identified by finding the descendants of all infections identified in the Systematized Nomenclature of Medicine--Clinical Terms (SNOMED CT) [8].

Antimicrobial prescribing for each PUS diagnosis was classified within a time-based framework corresponding to important branch points in antimicrobial decision-making that we termed Choice, Change, and Completion (CCC). Choice (i.e., the time during which decision-making centers around initial choice of empiric therapy) corresponded to the day of admission (day zero) followed by the next two calendar days of hospitalization (days 1-2). Change (i.e., the time in which antimicrobial therapy can be changed (de-escalated) based on microbiologic and other clinical data [9]) corresponded to days 3 and 4 of hospitalization. Completion (i.e., the time in which antibiotic selection is finalized and length of therapy is determined) corresponded to days 5 and 6 of hospitalization. Admission diagnoses were used to define PUS conditions to be included in Choice, while discharge diagnoses were used to define PUS conditions in Change and Completion. An additional measure termed duration of total antimicrobial therapy (DAT) included the entire course (inpatient and outpatient) of antimicrobial treatment if the PUS diagnosis was assigned at admission and discharge; this included the duration of inpatient therapy as well as the days supplied upon discharge. Validation of data capture for the Choice/Change/Completion-PUS framework was conducted via chart review at three of the intervention sites. At each site, one month of cases in which

a PUS diagnosis was identified were reviewed to ensure that antimicrobial therapy was captured appropriately in each CCC category. This validation uncovered occasional discrepancies that were clarified and refined in our coding.

Interactive antimicrobial graphic tool development, implementation, and evolution:

The first iteration of the antimicrobial graphic tools consisted of a web-based dashboard consisting of three interactive modules focusing on: a) overall trends in antimicrobial DOT/1000 DP, b) comparison of a single facility's SAARs to other facilities, and c) the proportion of patients receiving specific antibiotics at each of the CCC intervals for PUS diagnoses. Stewards had the ability to track their facility's antimicrobial use (overall, by class of drug, by SAAR category, by individual agent) according to month, quarter, or year stratified by ward type (medical/surgical ward versus intensive care unit). The second module showed the facility's SAARs on a bar graph as compared to other VA facilities that were sharing NHSN AU data, stratified by VA facility complexity [10]. The final module allowed stewards to see the frequency of their facility's use of any individual antimicrobial agent compared to all other VA facilities on the Choice/Change/Completion spectrum for PUS diagnoses in a box-and-whiskers plot, with the ability to stratify according to VA facility complexity and ward type (Figure 1).

The initial antimicrobial dashboards were implemented over an approximate 5-month time frame, between February and June 2016 at eight

VA facilities recruited by the investigators. Implementation at each site included a visit from study team members, with a kick-off lecture to medical staff promoting antimicrobial stewardship. We sought to involve at least one physician and one pharmacist steward at each site. Stewards were given data-viewing privileges specific to their institution prior to the site visit but were provided with additional instruction during the visit including how the data could be used to prioritize development of new stewardship interventions.

All eight sites subsequently underwent qualitative usability assessments of stewards' interactions with the antimicrobial dashboards via semi-structured interviews. Interviews focused on four areas: 1) the overall approach to stewardship of each ASP as well as types of stewardship activities; 2) a description of a specific experience using the antimicrobial dashboards; 3) user's perceived self-efficacy and knowledge regarding the concepts of Choice, Change and Completion, and 4) user's perceptions of usefulness and usability of the dashboards [11].

We held monthly learning collaborative calls with stewards and solicited feedback on how to improve the usability and interpretability of dashboard outputs. Stewards also shared "lessons learned" regarding effective use of the information gleaned from the antimicrobial use displays.

Based on feedback received through qualitative interviews and the monthly collaboratives we added several features to visual displays of antimicrobial trends, including facility-specific administration of the following

antimicrobial groups: 1) the 5 most commonly prescribed agents at the facility, 2) broad Gram-negative rod (GNR), 3) anti-staphylococcal, 4) anti-pseudomonal β -Lactams & anti-MRSA, 5) fluoroquinolone, and 6) antifungal therapies. Each display combined a line/bar graph of the facility's quarterly antimicrobial use over a 5 year period on the right side of the screen (with the ability to select any combination of intensive care unit (ICU), medical/surgical ward, and/or Community Living Center (i.e., VA nursing home), and a comparator graph on the left which displays aggregate VA-wide usage by selected facility complexity level (Figures 2a-c). Other dashboard tabs allow stewards to compare their facility's antimicrobial use by SAAR category (Figure 2d), CCC, and DAT for PUS conditions to all high-complexity (level 1A) VA facilities. Furthermore, the Pyramid Analytics (Kirkland, WA) platform allows for exportation of data into Microsoft Excel and graphs into figures that could be downloaded by stewards for presentation or local manipulation.

Standardized antimicrobial use report development:

In 2017 the interactive platform was supplemented by the development of pre-programmed static reports of antimicrobial use that retained many of the interactive dashboards' data comparisons. The pre-programmed version, though, allowed for updated reports to be automatically sent to stewards at user-defined intervals. When stewards signed up to receive the report, they had the ability to choose the complexity level of facilities to which their site would be compared and the frequency

with which and to whom the report is emailed. A sample static report, including a page on definitions is included as Appendix A.

Analysis of impact of program on antimicrobial use:

While local stewards were free to choose local interventions regarding what they perceived as their most pertinent antimicrobial usage issues, our analysis focused on three metrics that we hypothesized would be most affected by stewards' activities in using the graphic displays: 1) total inpatient use of all antimicrobials; 2) anti-MRSA agents (ceftaroline, dalbavancin, daptomycin, linezolid, oritavancin, quinupristin-dalfopristin, tedizolid, telavancin, intravenous vancomycin); and 3) anti-pseudomonal agents (amikacin, aztreonam, cefepime, ceftazidime, doripenem, gentamicin, imipenem-cilastatin, meropenem, piperacillin-tazobactam, tobramycin).

For these metrics, antimicrobial usage was calculated per DOT/1000 DP. Change in antimicrobial use over time was assessed with interrupted time series analysis pre- (January 2014 through January 2016) and post-intervention (July 2016 through January 2018), allowing for the 5-month implementation phase in between segments. We used generalized estimation equations with Poisson distribution to estimate the percentage difference in average monthly antimicrobial use rate between segments as a function of the intervention phase and intervention site indicator. Comparisons across facilities were conducted by aggregating data from the eight facilities and then analyzing these in relation to aggregated use across

all other VA facilities providing acute care services at an assigned complexity level that had available antimicrobial use data (n=118).

Results:

Steward insights and utility gained from the program:

During monthly collaborative calls, we asked stewards what specific insights and interventions were derived from interrogating the interactive graphic tools (selected examples in Table 1). Multiple sites focused on high utilization of anti-MRSA and anti-pseudomonal agents, especially during the Choice treatment phase and on the intensive care unit and surgical wards, prompting consideration of procalcitonin testing and timeout/reminder programs to encourage de-escalation. Fluoroquinolone usage and duration of therapy were other themes. One site that noted relatively high fluoroquinolone use and durations of therapy that prompted development of order sets that de-emphasized fluoroquinolones and creation of urinary antibiograms to assist with non-fluoroquinolone selection for UTI; a follow-up medication use evaluation at this site noted this intervention to be successful. Another site that had already transitioned much of its fluoroquinolone and antipseudomonal use to ceftriaxone used the tools to identify opportunities to de-escalate to narrower beta-lactams. Stewards also reported using different data reports in informal interactions with stakeholders (hospitalists, intensivists, surgeons, pharmacists, medical trainees) across their institutions. They also created reports and/or

presented data to formal committees within their facility (e.g., Pharmacy & Therapeutics, Infection Control, and Clinical Executive Boards). Throughout the post-intervention period where outcomes were assessed, participation in the monthly collaborative calls was 83% across all sites (range 65-100%). Pharmacists were the primary participants from 3 sites, physicians were primary participants from two sites, and pharmacists and physicians participated equally from 3 sites.

Changes in antimicrobial usage at program sites versus the rest of VA:

Intervention sites included seven level 1 and one level 2 complexity sites and had a median inpatient bed size of 151 (range 37-324), with a median ICU census of 14.4 (range 3.6 to 24.9) and medical-surgical bed size of 119.5 (range 37 to 246). The VA as a whole had a median inpatient bed size of 84 (range 4 to 367) with a median ICU census of 8.9 (range 1.0 to 26.9) and medical-surgical bed size of 76.5 (range 4 to 246). Changes in average monthly antimicrobial use at intervention and non-intervention VA facilities pre- and post-intervention are shown in Table 2. Intervention sites averaged a 2.1% decrease (95% CI [-5.7%, 1.6%], $p=0.2529$) in total antimicrobial use while non-intervention sites averaged a 2.5% increase (95% CI [0.8%, 4.1%], $p=0.0026$) in use pre- vs. post-intervention. The 4.6% absolute difference in change between intervention and non-intervention sites was statistically significant ($P=0.025$).

With regard to anti-MRSA antimicrobial use, intervention sites had an average 11.3% (95% CI [-16.0%, -6.3%], $p < 0.0001$) decrease and non-intervention sites had an average 6.6% decrease (95% CI [-9.1%, -3.9%], $P < 0.0001$) in anti-MRSA antimicrobial use pre- vs. post-intervention; the 4.7% change between the intervention and non-intervention sites showed only a statistical trend for significance ($P = 0.092$).

Finally, intervention sites had an average 3.4% (95% CI [-8.2%, 1.7%], $p = 0.185$) decrease in anti-pseudomonal antimicrobial use while non-intervention sites had an average 3.6% increase (95% CI [0.8%, 6.5%], $p = 0.011$); the 7.0% change between non-intervention and intervention sites was statistically significant ($P = 0.018$). We also performed a sensitivity analysis in which we included only level 1 complexity VA sites and excluded 45 sites of lower complexity (levels 2 and 3) from our controls and found nearly identical findings across all three outcomes (data not shown).

Variation among intervention sites in changes in antimicrobial use

The variation in changes in total, anti-MRSA, and antipseudomonal use according to individual intervention sites is shown in Figure 3. Changes were largely consistent across sites; however, sites C and H did not observe as consistent reductions in antimicrobial use as the others. Notably, site C had the lowest participation in the monthly collaboratives (65%) and site H experienced the sudden loss of its stewardship pharmacist early in the intervention period.

Discussion:

We developed and deployed interactive and standardized graphic tools at eight VA sites, allowing stewards to assess facility-level antimicrobial use overall, by drug class, for specific disease conditions, and over the course of therapy. These tools illustrated temporal trends in use and provided detailed comparisons with other similar VA facilities. Despite not proscriptively requiring stewards to focus on specific antimicrobial use policies, we found reductions in overall antimicrobial and anti-pseudomonal use relative to uninvolved facilities as well as a large absolute decrease in anti-MRSA antimicrobial use.

While we cannot directly attribute the decreases in antimicrobial use to stewards' use of the antimicrobial graphic tools, we hypothesize that the overall implementation strategy and follow-up served to activate stewards to pursue interventions that focused on the particular needs of their facilities. Inability to easily get data regarding local antimicrobial use patterns has long been recognized as a barrier to effective stewardship [12–14], and providing meaningful standardized metrics to individual facilities within a multihospital setting can be very challenging[15]. Furthermore, recent efforts to provide antimicrobial use data have focused on raw facility-specific numbers from the AU Option and standardized benchmarking data via SAAR and other observed-to-expected metrics [16] but do not provide comparative data showing inter-facility variability of antimicrobial use that may be important in

“nudging” stewards to devise interventions targeted to their facility. Rather than applying a “one-size-fits-all” approach to providing actionable metrics for ASPs, we allowed for customization of data receipt and presentation that can support the distinct local needs of any facility.

The most novel aspect of this work was the creation of the Choice/Change/Completion framework as a tool to evaluate where in the typical timeline of hospitalization for acute infectious conditions a facility may be overly broad in its antimicrobial prescribing patterns. This framework thematically resembles the four moments of antibiotic decision making recently described by Tamma, *et al*: 1) “Does this patient have an infection that requires antibiotics?” 2) “Have I ordered appropriate cultures before starting antibiotics?” 3) “A day or more has passed. Can I stop antibiotics?” and 4) “What duration of antibiotic therapy is needed for this patient’s diagnosis?”[18] Here, though, we apply a population-based quantitative determination of antimicrobial usage within discrete time frames in which decision making evolves to allow comparison of these decision points in aggregate across facilities as well as within a facility over time.

We also capture the total duration of antimicrobial therapy prescribed for common infectious syndromes, including antibiotics prescribed at hospital discharge. The post-discharge course may be particularly ripe for antimicrobial stewardship interventions, as highlighted by a recent study of an antimicrobial stewardship intervention to reduce inappropriate

fluoroquinolone prescription in 48 Michigan hospitals in which significant reductions in inpatient fluoroquinolone use were offset by twice as many new fluoroquinolone starts after discharge [19].

Limitations of our work include the relatively small number of sites involved (which were not selected at random and included the authors' own sites) and the bundling of the visual tools with the learning collaborative that does not allow for analysis of the effect of each individual component of the intervention. We also utilized a relatively simple statistical analysis of pre- and post-intervention antimicrobial utilization in which residual confounding may not have been fully captured. Furthermore, the exact relationship between amount of antimicrobial use and quality of infectious diseases management is unknown, though results from multiple VA analyses of antimicrobial utilization for pneumonia and other common infectious conditions indicate that opportunities to reduce excessive antimicrobial usage within the VA system remain ample [20–23]. Finally, our CCC paradigm only captures infections present at admission; antimicrobial utilization for infections acquired after hospital admission are not captured, and their treatment may interfere with our ability to measure antimicrobial usage for infections present at hospital admission if the antimicrobial course for the hospital-onset infection overlaps with that of the admission infection.

Anti-MRSA agent usage decreased throughout the VA over the timeframe of the study as compared to overall and antipseudomonal use, despite the fact that interventions targeting both anti-MRSA and

antipseudomonal use have been championed by the VA Antimicrobial Stewardship Task Force (Kelly ICHE paper). We noticed in a prior project that it was easier to show sustained decreases in vancomycin use with a timeout intervention than for piperacillin-tazobactam (J Hosp Pharm paper). It may very well be that, from a stewardship perspective, it is easier to operationalize discontinuation of anti-MRSA therapy (particularly in the VA where there is nasal colonization data that can help guide discontinuation) than antipseudomonal therapy. Thus, giving stewards more nuanced comparative data regarding their facility's antipseudomonal usage as was done in our current work may help them address this higher-hanging fruit.

In summary, while we were able to show temporal improvements in antimicrobial utilization in concert with our intervention, more research is needed on how visual graphics of population-level data can be used to influence prescribing patterns at a systems level. At minimum, our work also lends credence to the role that peer comparison can play in influencing prescribing changes on a facility level (in addition to what has been demonstrated for individual providers [24]). More broadly, we demonstrate the potential value to VA and other large healthcare delivery organizations of providing stewards with robust data on their facility's antimicrobial utilization. Finally, we hope that the Choice/Change/Completion framework we developed in this work can become a useful tool for antimicrobial stewardship clinical and research communities interested in defining

opportunities for improved prescribing across the time course of inpatient hospitalization.

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Table 1: Examples of areas for potential improvement identified by stewards and interventions considered or developed

<u>Area for improvement</u>	<u>Intervention</u>
High utilization of anti-MRSA and anti-pseudomonal agents at Choice	a) Introduction of serial procalcitonin testing for patients with suspected sepsis or lower respiratory tract infection b) Timeout program to encourage de-escalation
High fluoroquinolone utilization	a) Creation and evaluation of treatment pathways and order sets that de-emphasize fluoroquinolone use b) Creation of urinary antibiogram to assist in selection of non-fluoroquinolone options
Anti-pseudomonal agent utilization in SSTI	Pilot program in which providers who use anti-pseudomonal agents for SSTI are emailed reminders as to the proper indications for their use in SSTI
Excessive duration of therapy	Development of syndrome-specific treatment pathways

Table 2: Changes in average monthly antimicrobial use (DOT/1000 DP) at intervention and non-intervention VA facilities pre- and post-intervention

	Intervention sites (n=8)						Non-intervention sites (n=118)						p-value
	Pre	95% CI*	Post	95% CI	% change	p-value	Pre	95% CI	Post	95% CI	% change	p-value	
Total	474		471				526		541				
	53	-		-			54	-		-	+2.5%		0.02
	3	599-79	522	578-71	-2.1%	0.25	8	572-97	562	583-91	%	0.0026	-4.6%
Anti-MRSA	10					<0.00	10						0.09
	2	132-96	91	97	11.3%	01	5	113-123	98	105-128	-6.6%	01	-5.2%
Anti-pseudomonal	11	143		92-			13	-		-	+3.6%		0.01
	7		113	139	-3.4%	0.185	3	144	138	149	%	0.011	-7.0%

*: 95% Confidence Interval

Figure 1: Example of Choice/Change/Completion box and whisker plots*

*: sample facility's medical-surgical ward usage of piperacillin-tazobactam for pneumonia is denoted by small square; dotted line represents 50th percentile for all facilities compared; box represents 25th-75th percentile; whiskers represent 5th-95th percentile_

Figure 2: Interactive antimicrobial use dashboard examples

A: Overview/Overall Antimicrobial Use (Intensive Care Unit):*

B: Top Five Most Utilized Agents (Intensive Care Unit):

C: Pseudomonal β -Lactams and Anti-MRSA Therapy

D: Facility Variation Across SAAR Antibiotic Groups

*The yellow bars represent overall antimicrobial use (corresponding to the scale on the right of each figure). The lines represent antimicrobial use in each CDC SAAR group (corresponding to the scale on the left of each figure)

Figure 3: Variation among intervention sites in changes in antimicrobial use outcomes

Appendix A: Sample Summary Antimicrobial Use Email Report